

## ATTACHMENT B

### REMARKS

By this amendment, Applicants have amended the claims in a manner which now places this application in condition for allowance. In particular, a new set of claims is provided which includes claims 24-32 directed to methods for preparing a glycoalkaloid preparation that is essentially free of free sugars derived from the glycoalkaloids. Support for new claim 24 can be found throughout the original application, and also specifically in original claim 14. The principle difference between original claim 14 and new claim 24 is that new claim 24 is not limited to glycoalkaloids extracted from plant material. Support for glycoalkaloids from sources other than plant material may be found throughout the description, e.g., at lines 6-20 on page 11 and lines 9-17 on page 12. Applicants submit that as supported by the specification, the method of the present invention is not limited to glycoalkaloids derived from plant sources.

Other claim amendments include the addition of new claim 33 which corresponds to old claim 14 and thus derives support therefrom. New claims 33 and 54 are directed to a glycoalkaloid preparation produced according to the methods defined in claim 24 and 43, respectively, and claims 34 and 55 are directed to a medicinal compositions comprising said glycoalkaloid preparations. Finally, new claims 42 and 63 are directed to a method of treatment or control of cancer utilizing the medicinal composition of claims 34 and 55, respectively. Again, support for these claims may be found throughout the original specification including the original claim set, and in particular, medical composition claims 34 and 55 correspond to original claim 1, and method claims 42 and 63 correspond to original claim 23. Accordingly, no new matter has been entered.

The above amendments have been made entirely without prejudice and only to move this case along to allowance at the earliest possible time, and Applicant submits that the present claims place this case in condition for allowance for the reasons as set forth in detail below.

In the outstanding Official Action in the parent case, the Examiner contended that the claims were invalid under 35 U.S.C. § 112, first paragraph, on the grounds of lack of enablement. This rejection, insofar as applied to the claims as amended, is respectfully traversed for the reasons as set forth below.

In the present claims, the objection to prior Claim 23 has been rendered moot because in the amended claim, set new claims 42 and 63 have been limited to a method for the treatment or control of cancer that the examiner concedes as being enabled by the specification. The enablement objection raised against old claim 29 is also rendered moot as this claim has been deleted from the application.

In the outstanding Official Action in the parent case, the Examiner contended that the claims were indefinite under 35 U.S.C. § 112, second paragraph, on the grounds of lack of enablement. This rejection, insofar as applied to the claims as amended, is respectfully traversed for the reasons as set forth below.

In the first instance, the Examiner objected to the term "carbohydrate derivative". Applicant submits that this term has a clear and definite meaning to one skilled in the art and thus does not render the claims indefinite as alleged by the examiner. Preferred carbohydrate derivatives are provided on page 9, lines 4-14 and although this information is not required by a skilled person to understand the scope of the term "carbohydrate derivative" this information nevertheless provides additional information

as to what is included within the scope of the term. Reconsideration and withdrawal of this objection is respectfully requested.

With regard to the objection based on alleged improper Markush terminology, the examiner will note that the claims have been amended to recite the wording suggested by the examiner. Similarly, the objection against claim 2 based on the use of the phrase "eg" has been attended to by amendment of the claims. Finally, the objection insofar as it relates to original claim 23 has been rendered moot by the amendments made to the claims. The same comments apply in relation to the double-patenting objection raised against claim 23 in light of US 5,958,770. Applicant thus submits that the case is now entirely proper under 35 U.S.C. § 112 and that the Examiner's objections on the basis of this provision should be withdrawn.

Finally, in the parent case, the application was rejected on the basis that the claims lack novelty and/or are obvious in view of:

- (i) Cham *et al* (Cancer Letters, 55 (1990) 221-225);
- (ii) Australian patent 540812 (57853/80); and
- (iii) WO 91/10743.

These rejections, insofar as applied to the claims as amended, are respectfully traversed for at least the reasons set forth below.

In the first place, Applicant notes that the examiner alleges that the claims in the present application lack novelty in light of the BEC preparations described in the cited prior art before suffering from degradation. Please note that from a technical viewpoint, the BEC preparations in the prior art contain free sugars at the outset as these are one of the components of BEC resulting from the process used to produce BEC from plant material. Thus, it is incorrect to state that the washed preparations described in the present application encompass BEC "before such degradation occurs" as suggested by

the examiner. Moreover, in any event, the examiner will note that the claims of the present application have been limited to a method of preparing glycoalkaloid preparations including the step of removing "essentially all free sugars derived from the glycoalkaloid". No such method is taught or even remotely suggested in the cited prior art.

Further, with regard to the examiner's query in relation to the use of the term "essentially", we submit that it is not necessary for the specification to define this term for it to have a clear meaning to one skilled in the art. In this regard, the scope and meaning of the term "essentially" is clear when read in conjunction with the remainder of the specification and in light of the nature of the invention claimed in the present application. The object of the present invention is to increase the activity of glycoalkaloid compositions by removing the free sugars that, surprisingly, have been found to inhibit activity. The inhibitory activity of the free sugars is clearly illustrated in the examples provided in the specification and in particular examples 7 and 8. Although it would be ideal for all free sugars to be removed from the compositions, this may not be practically achievable in all circumstances. What is achievable using the method of the present invention is that the activity of the preparations can be increased by the "washing" process. Thus, we submit that it is clear that the term "essentially" as used in the present specification relates to removal of sufficient free sugars from the preparation to improve the composition's activity., and that this term would be readily understood as such by one of ordinary skill in the art,

The examiner also alleges that the prior art discloses that rhamnose inhibits the activity of BEC and this information renders the claims of the present application obvious as "a person having ordinary skill in the art at the time the instant invention was

made would have been motivated to remove even a trace amount of rhamnose from the BEC mixture in order to improve its activity". However, contrary to the Examiner's allegations, the above statement does not pay adequate attention to the nature of the present invention and in particular the nature of the problem it addresses. As the examiner will be aware, an invention can reside, at least partially, in the recognition/identification of a problem that was previously unknown and thus not addressed by the prior art. Once this problem is identified, the solution may be relatively straightforward, but this does not mean the invention itself is obvious.

In the present instance, at the time the instant invention was made the inhibitory effect of the free sugars resulting from the degradation of the glycoalkaloids in BEC was unknown. Given that the problem was unknown there cannot have been any motivation, as suggested by the Examiner, by a person of ordinary skill in the art to seek to apply the methods of the present invention to remove these free sugars and thus improve the activity of the compositions. Put another way, the cited art does not in any way disclose the problem addressed by the present invention. Rather, the studies concerning rhamnose in the cited art were conducted to learn more about the nature of the binding of the active agent to the cancer cells and established that the binding "may be mediated through the monosaccharide rhamnose" (see summary in the Cham *et al* Cancer Letters publication). The cited art does not disclose that degradation products in BEC inhibit its activity. It only teaches that when BEC is administered in conjunction with rhamnose its ability to prevent the death of mice suffering from cancer is decreased.

Accordingly, the different nature/intention of the prior art methods is reinforced by the fact that the amounts of rhamnose added to the BEC in the prior art methods far

exceeds the amount of free sugars removed by the methods of the present invention. Rhamnose at 5, 10 and 15 mg/kg of animal weight were added in the prior art methods whereas BEC at 8mg/kg of animal weight only has 1.48 mg/kg of rhamnose as part of the glycoalkaloid in the BEC. In short, the teachings of the prior art do not render the present invention obvious because they in no way disclose the problem addressed by the subject invention and thus cannot in any way represent a motivation or suggestion to a person skilled in the art to subject BEC preparations to the method of the present invention and thus improve their activity.

Applicant thus submits that the present invention is clearly not disclosed or suggested in the prior art, and that the rejections on the basis of the cited references are respectfully traversed and should be withdrawn.

In light of the amendments and arguments as set forth above, Applicants submit that the present application overcomes all prior rejections and has been placed in condition for allowance. Such action is earnestly solicited.

**END REMARKS**